THE AUTHORS REPLY

We appreciate the interest of McClelland et al. (1) in our recent analysis suggesting no association between women’s intravaginal practices and incident human immunodeficiency virus (HIV) infection (2).

Although a number of cross-sectional studies have suggested that intravaginal practices are associated with prevalent HIV infection, few data from prospective studies support an association with incident HIV (3). In addition to our study, van de Wijgert et al. (4) recently reported finding no association in a large cohort of women from the general population (i.e., non-sex workers) at several sites across sub-Saharan Africa. To our knowledge, McClelland et al.’s study of sex workers in Mombasa, Kenya (5) is the only prospective study to have found statistically significant associations after adjustment for relevant behavioral and biologic confounders.

McClelland et al. suggest that nondifferential misclassification of exposure due to less frequent study visits in our analysis (every 6–12 months) as compared with their analysis (every month) may explain the differing results (1). We think this comment is misleading. The exposure variable used in almost all of their analyses was one based on a single, composite measure of intravaginal practices at baseline; the outcome used in their analysis was subsequent newly detected HIV seropositivity over 10 years of follow-up. They did not provide data on associations between monthly intravaginal practice measures and HIV seroconversion, although this information was available for part of the cohort (5). Thus, their approach was very similar to ours and could not plausibly have led to the observed differences in study results. Moreover, it is unclear whether there is sufficient intraindividual variability in intravaginal practices over short time periods to make a monthly analysis any more informative than the one both groups of researchers adopted, and the timing of HIV acquisition could not have been established with such precision given the standard antibody tests used in both studies. In addition, McClelland et al.’s comment regarding the differences in HIV incidence between the two cohorts (1) does not have any relevance to the presence or absence of a causal association between intravaginal practices and HIV.

Of greater concern is the nature of intravaginal practices in the Mombasa cohort. Almost 95 percent of this group of approximately 1,200 sex workers reported intravaginal practices (5). This is among the highest prevalence of intravaginal practices documented in sub-Saharan Africa (3). The high prevalence of the exposure raises questions about the generalizability of the small “unexposed” reference group and limits the capacity to adequately adjust for confounding. Furthermore, McClelland et al. provided no data on the frequency or duration of intravaginal practices in their cohort, the proximity to sexual intercourse, or the incidence of HIV associated with specific practices (other than the two broad categories provided), making it more difficult to judge the plausibility of their suggestion of a causal association between intravaginal practices measured at enrollment and later HIV incidence.
We agree that further research into intravaginal practices and women’s risk of HIV acquisition should include attention to potential causal mechanisms, particularly variations in vaginal flora which may be caused by intravaginal practices. Previously, we demonstrated an association between bacterial vaginosis and risk of HIV acquisition in this cohort (6) but found no association between intravaginal practices and bacterial vaginosis. Data from sub-Saharan Africa on the associations between intravaginal practices and vaginal flora are similarly mixed (3), and more research into this question is clearly required.

Additional analyses of data from the Mombasa cohort have identified other risk factors for HIV acquisition that have not been borne out in larger population-based studies, most recently the findings for hormonal contraceptive use (7–10). This may be due to the unique nature of these cohort participants or the context of female sex work in Mombasa. More generally, we believe that it may be unwise to postulate a single, universal association involving an exposure which is known to be highly heterogeneous within and between populations. The specific types of intravaginal practices undertaken in these two cohorts, and across populations around the world, are likely to differ substantially. There is also considerable variation within populations in the types and frequency of such behaviors. This diversity means that a single global association between the broad construct of “vaginal washing” and HIV risk is unlikely.

Lack of consistency of associations across studies does not rule out true causal associations, but it does call the possibility of causality into question. We believe it may be more useful to focus on the possible heterogeneity of such practices to try to distinguish which ones might be relevant to HIV susceptibility.

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REFERENCES


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